REMARKS

Favorable reconsideration of this application, as presently amended and in light of the following discussion, is respectfully requested.

Claims 1,3-8 and 13-17 are pending in the present application. Claims 1, 4, 13 and 15-17 have been amended. The title was amended to correct a minor typographical error.

Applicants thank the Examiner for the courtesy of an interview extended to Applicants' representatives on July 17, 2008. During the interview, differences between the present invention and the applied art, and the rejections noted in the outstanding Office Action were discussed. No agreement was reached pending the Examiner's further review when a response is filed. Arguments presented during the interview are reiterated below.

In the outstanding Office Action, Claims 1, 3-7 and 13-17 were rejected under 35 U.S.C. § 101 as directed towards non-statutory subject matter; Claims 1, 3-7 and 13-17 were rejected under 35 U.S.C. § 103(a) as unpatentable over Quackenbush (Nature Reviews Genetics (2001), volume 2, pp. 418-427) in view of Getz et al. (PNAS (2000), volume 97, number 22, pp. 12079-84, herein "Getz"), Dougherty et al. (Journal of Computation Biology (January 2002), volume 9, number 1, pp. 105-126, herein "Dougherty") and Tolley (U.S. Publication No. 2004/0128080).

Regarding the rejection of Claims 1, 3-7 and 13-17 under 35 U.S.C. § 101, Claims 1, 13, 15, 16 and 17 were modified in light of the comments noted in the outstanding Office Action. Accordingly, it is respectfully requested this rejection be withdrawn.

Claims 1, 3-7 and 13-17 were rejected under 35 U.S.C. § 103(a) as unpatentable over Quackenbush in view of Getz, Dougherty and Tolley. That rejection is respectfully traversed.

Amended independent Claim 1 is directed to a method for identifying groups of co-regulated and co-expressed genes. The method includes defining a clustering criterion of data, relating to gene expression that varies with time and/or with the changing of environmental conditions, which is stored in a table, in function of said clustering criterion, identifying in sub-tables groups of genes that satisfy said clustering criterion, defining a number of logic

filtering criteria of the data of said table, for each logic filtering criterion, generating a corresponding filtered sub-table containing data of genes having expression values which satisfy said logic filtering criterion, establishing pair combinations of said sub-tables by clustering and filtering the data of said table with said filtering criteria and by said clustering, calculating characteristic parameters of the data associated to the groups of genes of each pair combination, generating for each pair combination a characteristic value in function of the characteristic parameters of the groups of genes by a decision algorithm based on soft computing techniques, identifying the groups of genes associated with pair combinations whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes involved in a particular cellular process and discarding pair combinations of groups of genes whose characteristic value is smaller than said threshold, and outputting to a user the group of genes within the pair combinations having characteristic values greater than the threshold in a selected data format.

Similarly, claim 13 includes representing characteristic parameters of data associated to genes of a pair of sub-tables which express correlation among and between included genes, and generating for each pair of sub-tables a characteristic value determined as a function of the characteristic parameters and outputting to a user the groups of genes within each pair of sub-tables whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes involved in a particular cellular process.

Claim 15 includes calculating a characteristic value for a cluster pair combination as a function of a plurality of characteristic parameters determined for each cluster pair which express a level of correlation which exists among and between the genes included in that cluster pair combination, identifying the genes associated with cluster pair combinations whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes involved in a particular cellular process, and outputting to a user the genes within the cluster pair combinations identified as being members of the network in a selected data format.

Claim 16 includes calculating a characteristic value for a pair combination as a function of a plurality of characteristic parameters determined for each pair combination which express a

level of correlation which exists among and between the genes included in that pair combination, identifying the genes associated with pair combinations whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes involved in a particular cellular process, and outputting to a user the genes within the pair combinations identified as being members of the network in a selected data format.

Claim 17 includes processing signals representative of characteristic parameters to generate for each pair of sub-tables a characteristic value determined as a function of the characteristic parameters, identifying groups of genes from each pair of sub-tables whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes involved in a particular cellular process, and outputting to a user data in a selected format including the groups of genes within each pair of sub-tables identified as being members of the network of genes.

After execution of the clustering algorithm, the present invention can recognize genes belonging to two different clusters (because of the adopted clustering criteria) which nonetheless belong to the same gene network (e.g., a group of co-expressed or co-regulated genes). Unlike the present invention, Quackenbush does not teach or suggest identifying groups of genes belonging to one or more clusters after execution of a clustering algorithm.

Additionally, the present invention recognizes that genes belonging to two different clusters belong to a same gene network if the characteristic parameter of the considered pair of clusters is lager than a certain threshold. Considering that the metric distance between the two clusters must obviously be much larger than the pre-established threshold distance disclosed by the present invention, the characteristic parameter of the present invention cannot be equivalent to the metric distance disclosed by Quackenbush.

Quackenbush discloses a typical hierarchical clustering algorithm (page 422) in which genes are clustered together if their metric distance (page 421, box 2) is smaller than a certain pre-established threshold distance. As such, the algorithm disclosed by Quackenbush generates clusters of genes that cannot be further grouped together because their metric distance is larger than the threshold distance.

Further, Claim 1 requires, *inter alia*, "identifying in sub-tables groups of genes that satisfy said clustering criterion" and "generating a corresponding filtered sub-table containing data of genes having expression values which satisfy said logic filtering criterion" and "establishing pair combinations of said sub-tables." Thus, claim 1 requires filtered sub-tables, wherein each sub-table includes genes which have satisfied certain logic filtering criteria. Claim 1 still further requires that plural pair combinations of sub-tables be established (*i.e.*, combined pairs of gene sub-tables).

With reference to Getz page 12079, left column, Getz summarizes the disclosed "philosophy." Getz states that "We look for pairs of a relatively small subset F_i of features (either genes or samples) and of objects O_j, (samples or genes), such that when the objects in O_j are represented using only the features from F_i, clustering yields stable and significant partitions." Applicants submit that this teaching of Getz relates to the distinct formation of a subset of genes (g) and a subset of samples (s). This teaching, by itself, fails to reach all of the claim limitations concerning the sub-tables and pair combinations of sub-tables. The reason for this is that Applicants specifically claim "establishing pair combinations of said sub-tables." By this it is meant pairs of sub-tables in combination, wherein each of the included sub-tables in the pair combination "contain[s] data of genes having expression values which satisfy said logic filtering criterion." This would be combined pairs of gene sub-tables. Getz, through his pairing operation associates (or pairs) features or objects. Thus, Getz's pairs include, for example, clustered genes, which are analogous to Applicants' sub-tables. Getz does not go the additional step recited by Applicants in claim 1 of pairing (gene) sub-tables in a pair combination. Getz fails to teach or suggest combining in pairs different clusters (sub-tables) of genes.

Getz teaches on page 12080 distinctly forming a stable subset of samples and a stable subset of genes. A pair is created from the combination of a sample subset (s) and a gene subset (g). This would be a sample/gene pair combination. This is not a teaching, however, of the claimed invention which "establish[es] pair combinations of said sub-tables" wherein each sub-table "contain[s] data of genes having expression values which satisfy said logic filtering criterion." Pairing in Getz always involves a sample subset (s) and a gene subset (g), and never, as is claimed by Applicants, pairs of gene sub-tables.

Applicants further note that Getz teaches the performance of an iterative clustering process. For example, the abstract recites "an algorithm, based on iterative clustering." Further, page 12080, left column, paragraph 2, states with respect to clustering that "These steps are iterated further ...." This iterative process disclosed in Getz for clustering is quite different from the claimed process recited in claim 1 which the clustering process is performed just once on the data. No iterative clustering operation is performed. Once the sub-tables are formed by clustering, as claimed, the process moves on to the formation of pair combinations of sub-tables. This is distinct from Getz which teaches starting from a parent pair (g, s), and then iteratively progressing from the parent to additional pairs (g, s) until no new clusters are found.

Claim 1 further recites "generating for each pair combination a characteristic value" and "identifying the groups of genes associated with pair combinations whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes." Applicants respectfully submit that Getz does not teach an operation to identify a group of genes "as being members of a network of genes." Rather, as taught by Getz on page 12080 (left column), applications of the Getz process allow for a) the "identif[ication of] genes that partition the samples according to a certain known classification of samples," b) the "discover[y of] new partitions," c) the "identif[ication of] subpartitions," and d) the revelation of "conditional correlations among genes." As recognized by those skilled in the art, none of these "applications" of the Getz process teaches "identifying the groups of genes associated with pair combinations ... as being members of a network of genes."

Applicants further point out that claim 1 also requires a certain threshold examination be performed. Claim 1 recites "generating for each pair combination a characteristic value" and "identifying the groups of genes associated with pair combinations whose characteristic value is greater than a certain pre-established threshold as being members of a network of genes." The Examiner points to the temperature threshold analysis described in Getz in the paragraph bridging pages 12080 and 12081. This temperature analysis, however, is related to the clustering process (SPC is a hierarchical clustering method), and not to any process for taking a characteristic value of a pair combination (gene sub-tables) and comparing that value against a threshold for determining membership in a network of genes as claimed by Applicants. This temperature teaching in the context of SPC clustering is simply irrelevant to the claimed

limitations for identifying members within a network of genes. The determination as to whether a stable cluster has been reached in Getz through temperature testing does not teach or suggest threshold analysis with respect to characteristic values of pair combinations of (gene) sub-tables and gene network membership.

Similar reasoning applies to independent claims 13 and 15-17.

Dougherty and Tolley do not overcome the above-identified deficiencies of Quackenbush and Getz.

In view of the foregoing, Applicants submit that claims 1, 13 and 15-17, and the claims dependent therefrom, distinguish over the cited prior art and are in condition for allowance.

Accordingly, it is respectfully requested this rejection be withdrawn.

CONCLUSION

In light of the arguments set forth above, Applicants respectfully submit that the Application is now in allowable form. Accordingly, Applicants respectfully request consideration and allowance of the currently pending claims.

Payment for a one-month extension of time fee of $120.00 is included with this Amendment. It is believed that no additional fees are due at this time. If this is incorrect, Applicants hereby authorize the Commissioner to charge any fees, other than issue fees, that may be required by this paper to Deposit Account No. 07-0153. The Examiner is respectfully requested to call Applicants' Attorney for any reason that would advance the current application to issue. Please reference Attorney Docket No. 364659-1003.

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Respectfully submitted,
GARDERE WYNNE SEWELL LLP

Karl L. Larson
Registration No. 41,141
ATTORNEY FOR APPLICANTS

3000 Thanksgiving Tower
1601 Elm Street
Dallas, Texas 75201-4761
(214) 999-4582 - Telephone
(214) 999-3623– Facsimile